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EXAMINER	
BALLARD, KIMBERLY	
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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,950	CARLSON ET AL.	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/16/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Claims 4-17 have been amended as requested in the preliminary amendment filed July 13, 2006. Following the amendment, claims 1-20 are pending in the present application.

2. Claims **1-20** are under consideration in the current office action.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on October 16, 2007 has been considered by the examiner.

Specification

4. The use of the trademark TACKTRAP has been noted in this application (page 18, line 16). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2, 3, 11-13, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claims 2, 11-13 and 18, the recitation of a “system" renders the claims indefinite because it is unclear whether the claims are drawn to a *method* or to an *apparatus* for determining whether a non-Drosophila odorant receptor binds to a test chemical. The metes and bounds of the claims thus cannot be determined.

8. Regarding claim 3, the conclusion step (i.e., determining whether the odorant receptor *binds* to the test chemical) does not achieve the goal set forth in the preamble (determining whether an odorant receptor *responds* to a test chemical) because the method steps do not specify that receptor binding is equivalent to measuring a receptor response. Therefore it is unclear whether the claim is directed to a method of determining an odorant receptor *response* or a method of determining odorant receptor *binding*, or whether a response encompasses binding. Thus, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-20 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 7,314,723 B2 to Zwiebel (issued January 1, 2008, earliest priority to January 26, 2001).

The claims are drawn to a *Drosophila* cell comprising an olfactory receptor neuron containing a non-*Drosophila* odorant receptor in place of its endogenous odorant receptor(s) (claim 1, 4-10 and 14-17), an *in vivo* system comprising said *Drosophila* cell for determining whether a non-*Drosophila* receptor binds to a test chemical, further comprising a test chemical (or mixture of two or more chemicals), a means of contacting the *Drosophila* cell with the test mixture and a means to measure the odor response of the neuron (claims 2, 11-13, and 18), and a method of determining whether an odorant receptor responds to a test chemical (claim 3) or binds to at least one chemical in a test mixture comprising two or more chemicals (claims 19-20).

Zwiebel teaches a method of identifying an agent which stimulates a mosquito odorant receptor when it is placed in a *Drosophila* host system (column 3, lines 11-14). The method includes, for example, expressing the mosquito (*Anopheles gambiae*) odorant receptor AgOR1 in *Drosophila* ab3 neurons using the bipartite Gal-UAS system to drive cell specific expression of the yeast transcription factor GAL4 (by the *Drosophila* Or22a promoter) which in turn activates the pUAST promoter upstream of AgOr1 in ab3A neurons in a Δhalo background (the Δhalo mutation deletes the endogenous

Or22a gene, such that Δhalo *Drosophila* mutants lack their endogenous Or22a odorant receptors) (see column 11, lines 16-47 and column 8, lines 16-21). These teachings would therefore anticipate limitations of instant claims 1, 4 (the neuron is a 3b3A neuron), 5 (a *Drosophila* fly comprises the cell), 6 (the endogenous odorant receptors are encoded by *Or22a* and *Or22b*), 7 (the non-*Drosophila* odorant receptor is from an insect that is a human pest), 8 (the non-*Drosophila* odorant receptor is isolated from an insect of the genus *Anopheles*), 9 (the non-*Drosophila* odorant receptor is encoded by *AgOr1* or *AgOr2*), 10 (the non-*Drosophila* odorant receptor is encoded by cDNA), and 14-17 (the gene encoding the non-*Drosophila* odorant receptor is operably linked to an *Or22a* promoter sequence, a *Gal4* sequence, and a *UAS* sequence).

Zwiebel further discloses that once the mosquito odorant receptor is expressed in a Drosophila system, agents can be identifying that modulate the neurons, such as by exposing the neuron to the agent, measuring an action potential of the neuron, and determining whether the agent modulates the neuron (column 3, lines 53-58). More specifically, ligands that bind to and modulate AgORs responses may be tested by these methods (see columns 9-10). For example, a panel of agents may be tested, such as candidate agents from human sweat and other human skin volatiles (column 9, lines 50-52), which address limitations in recited in instant claims 11 and 12. Zwiebel teaches that odor stimuli can be presented from Pasteur pipettes holding solutions of chemicals in paraffin oil on filter paper (column 13, lines 16-29), and responses from neurons can be made by extracellular electrophysiological recordings from live *Drosophila* (column 12, line 39 – column 13, line 15), such as by single-unit

electrophysiology (column 8, lines 36-37), thus meeting limitations of a “means of contacting the *Drosophila* cell with the test chemical” and a "means to measure the neuron response to the test chemical" of claims 2 and 18, as well as the recited limitation of claim 13. As such, the teachings of Zwiebel clearly anticipate claims 1-20.

11. Claims 1, 3, 5, 7, 8, 10, 15 and 16 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by US Patent 6,610,511 B1 to Carlson et al. (issued August 26, 2003, filed January 25, 2000).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Carlson et al. teach Drosophila odorant receptor proteins and methods of identifying agents which modulate the activity of an odorant receptor protein, such as by exposing cells which express the proteins to the agents and determining whether the agents modulate the activity of the proteins, thereby identifying agents which modulate the activity of the proteins (column 5, lines 24-33). Similarly, such methods can be used to identify binding partners for odorant receptor proteins (column 5, lines 45-52). Carlson et al. disclose that variants of the *Drosophila* odorant receptor (OR) proteins may be used in the above methods, including odorant receptor proteins such as from

insects from the genus *Anopheles* (column 9, lines 38-44 and 52-55). Carlson discloses that *Drosophila* cells can be transformed with a nucleic acid molecule that encodes an OR protein (column 14, lines 50-61). Further, Carlson teaches that transgenic insects containing mutant, knock-out or modified genes of the OR proteins of the invention, as well as transgenic insects into which recombinant, exogenous, or cloned genetic material has been experimentally transferred (column 24, lines 36-45), wherein the transferred genetic material (or "transgene") may consist of nucleic acid sequences derived from the genome of the same species or of a different species than the species of the target insect (column 24, lines 54-57). For example, a method making a transgenic *Drosophila* using P element mediated germline transformation is described in Example 6, columns 43-46. In this method, a coding sequence for a gene of interest is joined to an upstream activating sequence (UAS) and introduced by P element-mediated germline transformation into *Drosophila* using a yeast GAL4 transcription factor sequence coupled to a heat shock promoter, such as is recited in instant claims 15 and 16. Such introduced exogenous genetic material would be encoded by cDNA, thus meeting a limitation of claim 10. Additionally, the use of knock-out fruit flies is taught at column 28, lines 8-15, wherein Carlson notes that a "knock-out" generally refers to a mutant organisms which contain a null allele of a specific gene, such as specific odorant receptor genes of the disclosure.

Carlson further discloses that the present invention provides methods for identifying compounds which modulate insect behavior by exploiting the sensory capabilities of the target insect. For example, Carlson notes that it is possible to design

specific compounds which target mosquito olfactory receptor genes for the purpose of altering or eliminating the orientation and host-seeking feeding behaviors of mosquitoes, which would thereby have a positive impact on world health by controlling mosquito-borne diseases such as malaria (column 30, lines 11-24). It is noted that mosquitoes are a species from the genus *Anopheles* and are notoriously known for being pests to humans, thus meeting limitations of claims 7 and 8. Carlson teaches that the mosquito olfactory receptor genes may be used in various screening methods of the disclosure (such as are described above) to identify synthetic and natural compounds which may modulate the behavior of the insect. Taken together, the teachings provide for the expression of a mosquito odorant receptor in a transgenic Drosophila fly, such as a knock-out Drosophila, for use in the identification of compounds which modulate the response of the mosquito receptor. Accordingly, the teachings of Carlson et al. anticipate present claims 1, 3, 5, 7, 8, 10, 15 and 16.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being obvious over US Patent 6,610,511 B1 to Carlson et al. (issued August 26, 2003, filed January 25, 2000) in view of Fox et al. (*Proc Natl Acad Sci USA*, 2001; 98(25):14693-14697).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR

1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claim is drawn to a *Drosophila* cell comprising an olfactory receptor neuron containing a non-*Drosophila* odorant receptor in place of its endogenous odorant receptor(s), wherein the non-*Drosophila* odorant receptor is encoded by *AgOr1* or *AgOr2*.

The teachings of Carlson et al. are discussed above. Briefly, Carlson teaches the use of transgenic or knock-out *Drosophila* expressing a mosquito odorant receptor gene (i.e., a non-*Drosophila* odorant receptor in place of its endogenous odorant receptor, such as in the case of the knock-out *Drosophila*). The difference between the disclosure by Carlson et al. and that of the claimed invention is that the reference does not teach that the non-*Drosophila* odorant receptor is encoded by *AgOr1* or *AgOr2*.

Fox et al. teach the identification of odorant receptor genes from the mosquito *Anopheles gambiae*, which genes they have called *AgOr1*, *AgOr2*, *AgOr3*, and *AgOr4* (see p. 14694, 1st column). Fox notes that with the identification of these genes, functional, biochemical, behavioral, and transgenic studies may be undertaken to determine the specific classes of odorant ligands that activate these receptors. Additionally, Fox comments that by focusing on genes such as *AgOr1*, this process may

lend insight into the design of additional compounds that act as mosquito attractants or repellants (see p. 14697, 2nd column).

It would have been obvious to one of ordinary skill in the art at the time the invention was filed to replace the endogenous *Drosophila* odorant receptor gene with that of the mosquito *AgOr1* gene for use in the *Drosophila*-based screening methods taught by Carlson. The artisan would be motivated to use the *AgOr1* gene because both Carlson and Fox disclose that use of mosquito odorant receptors in transgenic studies would be useful for determining odorant ligands that could be used as mosquito attractants or repellants, thus influencing the behavior of the insect. Because such transformations are routinely undertaken in the art, particularly in the well-characterized *Drosophila* model, the artisan would reasonably expect that the *AgOr1* gene could be successfully expressed in a *Drosophila* cell. As such, the combined teachings of Carlson and Fox render obvious instant claim 9.

14. Claims 2, 11-13 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,610,511 B1 to Carlson et al. (issued August 26, 2003, filed January 25, 2000) in view of Fox et al. (*Proc Natl Acad Sci USA*, 2001; 98(25):14693-14697) as applied to claim 9 above, and further in view of De Bruyne et al. (*Neuron*, May 2001; 30:537-552; listed on IDS filed 10/16/2007) and Cork & Park (*Med Vet Entomol*. 1996; 10(3):269-276, Abstract only).

The teachings of the Carlson et al. and Fox et al. references are discussed above. While the prior art references do collectively teach a *Drosophila* cell comprising

an olfactory receptor neuron derived from a mosquito in place of its endogenous odorant receptor, the references do not teach a means of contacting the *Drosophila* cell with the test chemical and a means to measure the neuron response to the test chemical (as in claims 2 and 18). It is noted that such limitations ("means of" and "means to") have been interpreted as invoking 35 U.S.C. 112, sixth paragraph, and have been examined accordingly. The combined teachings of the prior art references also do not disclose that the test chemical is volatile or semi-volatile (as in claim 11), that the test chemical is a component of mammalian sweat (claim 12), that the odor response is measured by single-unit electrophysiology (claim 13), or that the test mixture comprises two or more chemicals (claims 18-20).

De Bruyne et al. teach a functional analysis of odor coding in the *Drosophila* antenna. Odorant receptors on Drosophila olfactory sensilla (structures on the antennae that comprise odorant receptor neurons) were stimulated by presentation of a panel of volatile test chemicals via a syringe containing odors dissolved in paraffin oil or water and, in some cases, applied to filter paper (see section on "Odor Stimulation" on p. 551). This is consistent with the instant specification's disclosure of odor stimuli presentation in Pasteur pipettes holding solutions of chemicals in paraffin oil on filter paper (see p. 24 of the specification). Further, De Bruyne et al. note that a 0.55 s stimulus period was used in all recordings employing a "syringe puff" method, which is equivalent to the instant specification's disclosure of a stimuli presented by directing an air stream to the fly to give a 0.5 s pulse of odor stimulus (see p. 24), which would meet the "means of contacting" limitation of claims 2 and 18. Additionally,

electrophysiological recordings of neurons comprising the odorant receptors were used in both the instant specification and the methods of De Bruyne, thus addressing the "means to measure" limitation of claims 2 and 18 and other recited limitations within claims 13 and 19.

As noted previously, a panel of various test chemicals was employed, either individually or in combination, to characterize the responses of the odorant receptor neurons. For example, De Bruyne teaches that the firing rate of a neuron was increased by exciting it with one odor, and then other odors were tested for their ability to decrease the firing rate of the excited neuron (see p. 542, 2nd column), which addresses recited limitations of claims 18-20 regarding "two or more chemicals". Finally, De Bruyne et al. comment that their *in vivo* system for the study of odor coding is attractive because 1) physiological recordings can be made from the odorant receptor neurons (ORNs) *in vivo*; 2) the fly's olfactory system is numerically simple; its ORNs can be classified into a limited number of distinct functional types; and 3) the results of physiological analysis can be integrated with the results of molecular, genetic, anatomical, and behavioral studies to construct an integrated model of odor coding (see p. 537, 2nd column).

Cork and Park teach the identification of various volatile compounds within human sweat and demonstrate that many of these compounds elicit responses from the antennae of female *Anopheles gambiae* mosquitoes, which are carriers of malaria. Intact antennae of the mosquito were stimulated with various compounds identified in the sweat fractions, which response to the compounds were measured by

electroantennography (EAG). Cork and Park note that two non-acidic compounds, 1-octen-3-ol and 4-methylphenol, were found to elicit significant dose-dependent EAG responses from female *A. gambiae*. It is noted that both of these compounds were also used by De Bruyne et al. in their odorant screening (see Table 1 on p. 543).

As evidenced by the prior art, the skilled artisan would have recognized the importance of identifying compounds that could either attract or repel the female mosquito *A. gambiae*, because this mosquito is known to spread malaria. Thus, it would have been obvious to one of skill in the art at the time the invention was filed to utilize the odor screening techniques taught by De Bruyne in an *in vivo* system that comprised a *Drosophila* cell containing a non-*Drosophila* odorant receptor, such as the *AgOr1* receptor from the mosquito *A. gambiae*, as taught by Carlson and Fox. Similarly, it would have been obvious to use two or more volatile or semi-volatile test compounds, such as those found in human sweat, which are particularly attractive to female *A. gambiae* mosquitoes, with the intent of identifying compounds that bind to *AgOr1* odorant receptor. This is because the skilled artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. De Bruyne et al. evidence that such techniques can be successfully used to elicit responses in individual neurons within the *Drosophila* antennae, and further note that such a system is advantageous for molecular, genetic and behavioral studies. And Carlson et al. disclose that transgenic *Drosophila* flies can be used to identify compounds that modulate the responses of the OR neurons, and the receptors contained therein. Thus, the artisan would reasonably expect that the test chemical presentation and neuronal

response measurement techniques taught by De Bruyne could be predictably used to identify chemical components derived from human sweat that bind to and elicit responses from mosquito ORs in an *in vivo Drosophila* model. Such would amount to combining prior art elements according to known methods to yield predictable results.

15. Claims 2, 4, 6, 11, 13, 14 and 17 are rejected under 35 U.S.C. 103(a) as being obvious over US Patent 6,610,511 B1 to Carlson et al. (issued August 26, 2003, filed January 25, 2000) in view of Dobritsa et al. (*Neuron*, March 6, 2003; 37:827-841).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Carlson et al. are summarized above. However, the Carlson et al. reference does not teach that the olfactory receptor neuron is an ab3A neuron (as in present claim 4), that the endogenous odorant receptors are encoded by *Or22a* and *Or22b* (claim 6), or that the gene encoding the non-*Drosophila* odorant receptor is operably linked to an *Or22a* promoter sequence (claim 14), a *Gal4* sequence, and a *UAS* sequence (claim 17). The reference by Carlson et al. also does not teach an *in vivo* system for determining whether a non-*Drosophila* odorant receptor binds to a test chemical comprising, *inter alia*, a means of contacting the *Drosophila* cell with the test chemical and a means to measure the neuron response to the test chemical (as in claim 2). It is noted that such limitations ("means of" and "means to") within claim 2 have been interpreted as invoking 35 U.S.C. 112, sixth paragraph.

Dobritsa et al. teach the production and functional characterization of a mutant *Drosophila* in which particular odorant receptors, *Or22a* and *Or22b*, have been deleted from the genome. In *Drosophila*, individual odorant receptors map to individual neuronal classes (see p. 827). In order to determine in which functional type or types of sensilla *Or22a/b* were expressed, Dobritsa et al. used an *Or22a* or *Or22b* promoter to drive expression of the yeast transcription factor *GAL4* under the control of an upstream activation sequence (*UAS*), which in turn drove expression of GFP (see 1st column, p. 830). This same configuration, *Or22a-GAL4; UAS* and *Or22b-GAL4; UAS*, was used to drive expression of the cell death gene *reaper* (*rpr*) in order to identify the specific neuronal cell type to which *Or22a/b* mapped (see 2nd column, p. 830, and p. 840, 1st column) and to express the antennal gene, Or47a (see p. 835). Dobritsa et al. report

that the both *Or22a* and *Or22b* map to ab3A neurons in the sensillum of *Drosophila*, and that in the absence of these genes, ab3A neurons do not respond to any of a wide variety of tested odors (1st column on p. 831), thus addressing present claim 4. Dobritsa used single-unit electrophysiology to measure the responses of the neurons, and presentation of odor stimuli from Pasteur pipettes holding solutions of chemicals in paraffin oil on filter paper (see p. 840), both techniques of which are consistent with the means of contacting the *Drosophila* cell and means for measuring the odor response disclosed in the instant specification (as in Example 4 at pp. 23-25), thus meeting limitations of claims 2 and 13. Additionally, the odors tested to elicit responses of the odorant receptors in the neurons were volatile chemicals (see, for example, Figures 3-6), thus addressing a recited limitation of claim 11. In summary, the teachings of Dobritsa et al. provide for a method to express particular genes of interest in an *in vivo* *Drosophila* system which contains no functional endogenous odorant receptors (called Δhalo mutants by the authors), and methods for testing and measuring responses of these neurons to various odorant stimuli.

It would have been obvious to one of skill in the art at the time the invention was filed to utilize the *in vivo* system as taught by Dobritsa et al. to measure responses of particular odorant receptors (such as those from mosquitoes) to various test chemicals, as is disclosed by Carlson et al. In order to assess whether a test chemical stimulates a particular odorant receptor, the skilled artisan would have recognized the benefit of expressing the odorant receptor in a system which lacks any (endogenous) odorant receptors. One of skill in the art would have therefore been motivated to take

advantage of the Δhalo strain of *Drosophila,* in which a chromosomal deletion has resulted in the loss of the endogenous receptors (*OR22a/b*) from the ab3A odorant receptor neurons. Moreover, Dobritsa et al. demonstrate the effectiveness of the disclosed techniques to express genes of interest in the ab3A neurons (using *Or22a-GAL4-UAS* expression sequences), expose the neurons to a panel of volatile and semi-volatile test chemicals, and measure the odorant receptor responses in the neurons using electrophysiology. Thus, the skilled artisan would have a reasonable expectation that expression of, for example, a mosquito odorant receptor in such an *in vivo* system and subsequent testing of the expressed odorant receptor would be successful. Accordingly, the combined teachings of the above references render obvious instant claims 2, 4, 6, 11, 13, 14 and 17.

Conclusion

16. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 9 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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